

Amendments to the Claims:

The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-148 (Cancelled)

149. (New) A method of screening for a compound that modulates sweet taste signaling in taste cells, the method comprising the steps of:

(i) contacting the compound with a hetero-oligomeric taste transduction G-protein coupled receptor that responds to sweet taste stimuli; wherein said hetero-oligomeric receptor comprises a polypeptide that is encoded by a nucleic acid sequence that specifically hybridizes under stringent hybridization conditions to a human T1R2 nucleic acid comprising the nucleotide sequence of SEQ ID NO:3, and further comprises a polypeptide that is encoded is by a nucleic acid sequence that specifically hybridizes under stringent hybridization conditions to the human T1R3 nucleotide sequence of SEQ ID NO: 5; wherein stringent hybridization conditions comprise conducting the hybridization reaction at 42°C in a solution comprising 50% formamide, 5 x SSC, and 1% SDS and washing at 65°C in a solution comprising 0.2 x SSC and 0.1% SDS; and

(ii) determining whether said compound binds to and/or affects the activity of said hetero-oligomeric sweet receptor.

150. (New) A method of screening for a compound that enhances or inhibits the binding to and/or activation of a sweet compound to a hetero-oligomeric taste transduction G-protein coupled receptor that responds to sweet taste stimuli, by a sweet compound the method comprising the steps of:

(i) contacting said hetero-oligomeric receptor with said compound and further contacting said hetero-oligomeric receptor with a sweet compound; wherein said hetero-oligomeric receptor comprises a polypeptide that is encoded by a nucleic acid sequence that specifically hybridizes under stringent hybridization conditions to the human T1R2 nucleotide sequence of SEQ ID NO:3 and further comprises a polypeptide encoded by a nucleic acid sequence that specifically hybridizes under stringent hybridization conditions to the human T1R3 nucleotide sequence of SEQ ID NO: 5; wherein stringent hybridization conditions comprise conducting the hybridization reaction at 42°C in a solution comprising 50% formamide, 5 x SSC, and 1% SDS and washing at 65°C in a solution comprising 0.2 x SSC and 0.1% SDS; and

(ii) determining the effect of said compound on the binding of said sweet compound to said hetero-oligomeric receptor and/or the activity of said hetero-oligomeric sweet receptor.

151. (New) The method of claim 149 wherein said hetero-oligomeric receptor is comprised on a membrane.

152. (New) The method of claim 150 wherein said hetero-oligomeric receptor is comprised on a membrane.

153. (New) The method of claim 149 wherein said hetero-oligomeric receptor is expressed by a cell.

154. (New) The method of claim 150 wherein said hetero-oligomeric receptor is expressed by a cell.

155. (New) The method of claim 153 wherein said cell is selected from the group consisting of bacteria, yeast insect, mammalian, amphibian and worm cells.

156. (New) The method of claim 154 wherein said cell is selected from the group consisting of bacteria, yeast, insect, mammalian, amphibian and worm cells.

157. (New) The method of claim 153 wherein said hetero-oligomeric receptor is expressed by a mammalian cell.

158. (New) The method of claim 154 wherein said hetero-oligomeric receptor is expressed by a mammalian cell.

159. (New) The method of claim 157 wherein said mammalian cell is selected from the group consisting of CH0, Hela and HEK-293 cells.

160. (New) The method of claim 158 wherein said mammalian cell is selected from the group consisting of CH0, Hela and HEK-293 cells.

161. (New) The method of claim 149 wherein the hetero-oligomeric receptor is linked to a solid phase.

162. (New) The method of claim 150 wherein the hetero-oligomeric receptor is linked to a solid phase.

163. (New) The method of claim 149 wherein the hetero-oligomeric receptor comprises an extracellular domain that is covalently linked to said receptor.
164. (New) The method of claim 150 wherein the hetero-oligomeric receptor comprises an extracellular domain that is covalently linked to said receptor.
165. (New) The method of claim 153 wherein said cell further expresses a G protein that couples to said hetero-oligomeric receptor.
166. (New) The method of claim 154 wherein said cell further expresses a G protein that couples to said hetero-oligomeric receptor.
167. (New) The method of claim 165 wherein said G protein is $G_{\alpha 15}$ or $G_{\alpha 16}$.
168. (New) The method of claim 166 wherein said G protein is $G_{\alpha 15}$ or $G_{\alpha 16}$.
169. (New) The method of claim 149 wherein the activity of said taste receptor is measured by detecting changes in intracellular Ca^{2+} levels.
170. (New) The method of claim 150 wherein the activity of said taste receptor is measured by detecting changes in intracellular Ca^{2+} levels.
171. (New) The method of claim 169 wherein Ca^{2+} levels are detected using an ion sensitive dye or a membrane voltage fluorescent indicator.
172. (New) The method of claim 170 wherein Ca^{2+} levels are detected using an ion sensitive dye or a membrane voltage fluorescent indicator.
173. (New) The method of claim 149 wherein taste receptor activity is detected by monitoring changes in ion polarization.
174. (New) The method of claim 150 wherein taste receptor activity is detected by monitoring changes in ion polarization.

175. (New) The method claim 149 wherein taste receptor activity is measured by detecting changes in second messenger levels.

176. (New) The method claim 150 wherein taste receptor activity is measured by detecting changes in second messenger levels.

177. (New) The method of claim 175 wherein said second messenger is IP3.

178. (New) The method of claim 176 wherein said second messenger is IP3.

179. (New) The method of claim 149 wherein taste receptor activity is measured by detecting changes in intracellular cyclic nucleotides.

180. (New) The method of claim 150 wherein taste receptor activity is measured by detecting changes in intracellular cyclic nucleotides.

181. (New) The method of claim 179 wherein said cyclic nucleotide is cAMP or cGMP.

182. (New) The method of claim 180 wherein said cyclic nucleotide is cAMP or cGMP.

183. (New) The method of claim 149 wherein taste receptor activity is detected by measuring changes in Ca^{2+} levels by fluorescence imaging.

184. (New) The method of claim 150 wherein taste receptor activity is detected by measuring changes in Ca^{2+} levels by fluorescence imaging.

185. (New) The method of claim 149 wherein changes in taste receptor activity are detected by measuring changes in G protein binding of $\text{GTP}\gamma\text{S}$.

186. (New) The method of claim 150 wherein changes in taste receptor activity are detected by measuring changes in G protein binding of $\text{GTP}\gamma\text{S}$.

187. (New) The method of claim 149 which is a high throughput screening assay.

188. (New) The method of claim 150 which is a high throughput screening assay.

189. (New) The method of claim 149 wherein said hetero-oligomeric taste receptor comprises the polypeptides encoded by SEQ ID NO: 3 and SEQ ID NO:5.

190. (New) The method of claim 150 wherein said hetero-oligomeric taste receptor is comprises the polypeptides encoded by SEQ ID NO: 3 and SEQ ID NO:5.

191. (New) The method of claim 149 wherein said hetero-oligomeric taste receptor binds to and/or is activated by a sweet ligand selected from the group consisting of cyclamate, sucrose, fructose, neotane, aspartame, saccharin and Acesulfane K.

192. (New) The method of claim 150 wherein said sweet compound is selected from the group consisting of cyclamate, sucrose, fructose, glucose, neotane, aspartame, saccharin and Acesulfane K.

193. (New) A method of screening for a compound that modulates sweet taste signaling in taste cells, the method comprising the steps of:

(i) contacting the compound with a hetero-oligomeric taste transduction G-protein coupled receptor that responds to sweet taste stimuli, wherein said hetero-oligomeric receptor comprises a T1R2 polypeptide that comprises at least 90% sequence identity to the polypeptide encoded by the

human T1R2 nucleic acid sequence of having SEQ ID NO:3, and further comprises a T1R3 polypeptide that comprises at least 90% sequence identity to the polypeptide encoded by the human T1R3 nucleic acid sequence having SEQ ID NO:5;

(ii) determining whether said compound binds to and/or affects to activity of said hetero-oligomeric sweet receptor.

194. (New) The method of claim 193 wherein said T1R2 polypeptide comprises at least 95% sequence identity to the polypeptide encoded by SEQ ID NO:3.

195. (New) The method of claim 193 wherein said T1R2 polypeptide comprises at least 95% sequence identity to the polypeptide encoded by SEQ ID NO:5.

196. (New) The method of claim 193 wherein said T1R2 polypeptide comprises at least 96% sequence identity to the polypeptide encoded by SEQ ID NO:3.

197. (New) The method of claim 193 wherein said T1R3 polypeptide comprises at least 96% sequence identity to the polypeptide encoded by SEQ ID NO:5.

198. The method of claim 193 wherein said T1R2 polypeptide comprises at least 97% sequence identity to the polypeptide encoded by SEQ ID NO:3.

199. (New) The method of claim 193 wherein said T1R3 polypeptide comprises at least 97% sequence identity to the polypeptide encoded by SEQ ID NO:5.

200. (New) The method of claim 193 wherein said T1R2 polypeptide comprises at least 98% sequence identity to the polypeptide encoded by SEQ ID NO:3.

201. (New) The method of claim 193 wherein said T1R3 polypeptide comprises at least 98% sequence identity to the polypeptide encoded by SEQ ID NO:5.

202. (New) The method of claim 193 wherein said T1R2 polypeptide comprises at least 99% sequence identity to the polypeptide encoded by SEQ ID NO:3.

203. (New) The method of claim 193 wherein said T1R3 polypeptide comprises at least 99% sequence identity to the polypeptide encoded by SEQ ID NO:5.

204. (New) The method of claim 193 wherein said T1R2 polypeptide has the polypeptide sequence encoded by SEQ ID NO:3.

205. (New) The method of claim 193 wherein said T1R3 polypeptide has the polypeptide sequence encoded by SEQ ID NO:5.

206. (New) The method of claim 193 wherein said T1R2 polypeptide has the polypeptide sequence encoded by SEQ ID NO:3 and said T1R3 polypeptide has the amino acid sequence encoded by SEQ ID NO:5.

207. (New) A method of screening for a compound that enhances or inhibits the binding to and/or activation of a sweet compound to a hetero-oligomeric taste transduction G-protein coupled receptor that responds to sweet taste stimuli, the method by a sweet compound comprising the steps of:

(i) contacting said hetero-oligomeric receptor with said compound and further contacting said hetero-oligomeric receptor with a sweet compound; wherein said hetero-oligomeric receptor comprises a T1R2 polypeptide that has at least 90% sequence identity to the T1R2 polypeptide encoded by SEQ ID NO:3 and further comprises a T1R3 polypeptide that has at least 90% sequence identity to the T1R3 polypeptide encoded by SEQ ID NO:5; and

(ii) determining the effect of said compound on the binding of said sweet compound to said hetero-oligomeric receptor and/or the activity of said hetero-oligomeric sweet receptor.

208. (New) The method of claim 207 wherein said T1R2 polypeptide comprises at least 95% sequence identity to the polypeptide encoded by SEQ ID NO:3.

209. (New) The method of claim 207 wherein said T1R2 polypeptide comprises at least 95% sequence identity to the polypeptide encoded by SEQ ID NO:5.

210. (New) The method of claim 207 wherein said T1R2 polypeptide comprises at least 96% sequence identity to the polypeptide encoded by SEQ ID NO:3.

211. (New) The method of claim 207 wherein said T1R3 polypeptide comprises at least 96% sequence identity to the polypeptide encoded by SEQ ID NO:5.

212. The method of claim 207 wherein said T1R2 polypeptide comprises at least 97% sequence identity to the polypeptide encoded by SEQ ID NO:3.

213. (New) The method of claim 207 wherein said T1R3 polypeptide comprises at least 97% sequence identity to the polypeptide encoded by SEQ ID NO:5.

214. (New) The method of claim 207 wherein said T1R2 polypeptide comprises at least 98% sequence identity to the polypeptide encoded by SEQ ID NO:3.

215. (New) The method of claim 207 wherein said T1R3 polypeptide comprises at least 98% sequence identity to the polypeptide encoded by SEQ ID NO:5.

216. (New) The method of claim 207 wherein said T1R2 polypeptide comprises at least 99% sequence identity to the polypeptide encoded by SEQ ID NO:3.

217. (New) The method of claim 207 wherein said T1R3 polypeptide comprises at least 99% sequence identity to the polypeptide encoded by SEQ ID NO:5.
218. (New) The method of claim 207 wherein said T1R2 polypeptide has the polypeptide sequence encoded by SEQ ID NO:3.
219. (New) The method of claim 207 wherein said T1R3 polypeptide has the polypeptide sequence encoded by SEQ ID NO:5.
220. (New) The method of claim 207 wherein said T1R2 polypeptide has the polypeptide sequence encoded by SEQ ID NO:3 and said T1R3 polypeptide has the amino acid sequence encoded by SEQ ID NO:5.
221. (New) The method of claim 193 wherein said hetero-oligomeric receptor is comprised on a membrane.
222. (New) The method of claim 207 wherein said hetero-oligomeric receptor is comprised on a membrane.
223. (New) The method of claim 193 wherein said hetero-oligomeric receptor is expressed by a cell.
224. (New) The method of claim 207 wherein said hetero-oligomeric receptor is expressed by a cell.
225. (New) The method of claim 223 wherein said cell is selected from the group consisting of bacteria, yeast insect, mammalian, amphibian and worm cells.

226. (New) The method of claim 224 wherein said cell is selected from the group consisting of bacteria, yeast, insect, mammalian, amphibian and worm cells.
227. (New) The method of claim 223 wherein said hetero-oligomeric receptor is expressed by a mammalian cell.
228. (New) The method of claim 224 wherein said hetero-oligomeric receptor is expressed by a mammalian cell.
229. (New) The method of claim 227 wherein said mammalian cell is selected from the group consisting of CHO, Hela and HEK-293 cells.
230. (New) The method of claim 228 wherein said mammalian cell is selected from the group consisting of CHO, Hela and HEK-293 cells.
231. (New) The method of claim 193 wherein the hetero-oligomeric receptor is linked to a solid phase.
232. (New) The method of claim 207 wherein the hetero-oligomeric receptor is linked to a solid phase.
233. (New) The method of claim 193 wherein the hetero-oligomeric receptor comprises an extracellular domain that is covalently linked to said receptor.
234. (New) The method of claim 207 wherein the hetero-oligomeric receptor comprises an extracellular domain that is covalently linked to said receptor.
235. (New) The method of claim 193 wherein said cell further expresses a G protein that couples to said hetero-oligomeric receptor.

236. (New) The method of claim 207 wherein said cell further expresses a G protein that couples to said hetero-oligomeric receptor.
237. (New) The method of claim 235 wherein said G protein is $G_{\alpha 15}$ or $G_{\alpha 16}$.
238. (New) The method of claim 236 wherein said G protein is $G_{\alpha 15}$ or $G_{\alpha 16}$.
239. (New) The method of claim 193 wherein the activity of said taste receptor is measured by detecting changes in intracellular Ca^{2+} levels.
240. (New) The method of claim 207 wherein the activity of said taste receptor is measured by detecting changes in intracellular Ca^{2+} levels.
241. (New) The method of claim 239 wherein Ca^{2+} levels are detected using an ion sensitive dye or a membrane voltage fluorescent indicator.
242. (New) The method of claim 240 wherein Ca^{2+} levels are detected using an ion sensitive dye or a membrane voltage fluorescent indicator.
243. (New) The method of claim 193 wherein taste receptor activity is detected by monitoring changes in ion polarization.
244. (New) The method of claim 207 wherein taste receptor activity is detected by monitoring changes in ion polarization.
245. (New) The method claim 193 wherein taste receptor activity is measured by detecting changes in second messenger levels.
246. (New) The method claim 207 wherein taste receptor activity is measured by detecting changes in second messenger levels.
247. (New) The method of claim 245 wherein said second messenger is IP3.
248. (New) The method of claim 246 wherein said second messenger is IP3.

249. (New) The method of claim 193 wherein taste receptor activity is measured by detecting changes in intracellular cyclic nucleotides.
250. (New) The method of claim 207 wherein taste receptor activity is measured by detecting changes in intracellular cyclic nucleotides.
251. (New) The method of claim 249 wherein said cyclic nucleotide is cAMP or cGMP.
252. (New) The method of claim 250 wherein said cyclic nucleotide is cAMP or cGMP.
253. (New) The method of claim 193 wherein taste receptor activity is detected by measuring changes in Ca^{2+} levels by fluorescence imaging.
254. (New) The method of claim 207 wherein taste receptor activity is detected by measuring changes in Ca^{2+} levels by fluorescence imaging.
255. (New) The method of claim 193 wherein changes in taste receptor activity are detected by measuring changes in G protein binding of $\text{GTP}\gamma\text{S}$.
256. (New) The method of claim 207 wherein changes in taste receptor activity are detected by measuring changes in G protein binding of $\text{GTP}\gamma\text{S}$.
257. (New) The method of claim 193 which is a high throughput screening assay.
258. (New) The method of claim 207 which is a high throughput screening assay.
259. (New) The method of claim 228 wherein said hetero-oligomeric taste receptor comprises the polypeptides encoded by SEQ ID NO: 3 and SEQ ID NO:5.

260. (New) The method of claim 229 wherein said hetero-oligomeric taste receptor comprises the polypeptides encoded by SEQ ID NO: 3 and SEQ ID NO:5.

261. (New) The method of claim 193 wherein said hetero-oligomeric taste receptor binds to and/or is activated by a sweet ligand selected from the group consisting of cyclamate, sucrose, fructose, neotane, aspartame, saccharin and Acesulfane K.

262. (New) The method of claim 207 wherein said known sweet compound is selected from the group consisting of cyclamate, sucrose, fructose, glucose, neotane, aspartame, saccharin and Acesulfane K.